REMARKS

Claims 80 and 81 are currently pending. Claims 51-79 are cancelled herein to advance prosecution and without prejudice to the prosecution of their subject matter in other patent applications.

Claim 80 is amended to require that any protein encoded by nucleic acid hybridizing to the protein-encoding region of SEQ ID NO:1 under stringent conditions *also* binds to an antibody directed toward the peptide fragment of SEQ ID NO:2 having the sequence Pro-Ser-Gln-Glu-Asn-Glu-Met-Phe-Ser-Ile-Arg-Asp (SEQ ID NO:5). This amendment is supported by the instant specification at paragraph 47, and therefore does not consistute new matter.

Claims 80 and 81 are amended to require that the therapeutic nucleic acids "are administered to the subject by a method selected from the group consisting of intra-tumor injection and instillation following surgical resection of a tumor into the tumor bed," which is supported by the instant specification at paragraphs 103 and 104, and therefore does not constitute new matter.

Claims 51-80 are rejected under the first paragraph of 35 U.S.C. §112 for allegedly failing to comply with the written description requirement.

Claims 51-81 are rejected under the first paragraph of 35 U.S.C. §112 for allegedly lacking enablement for the full scope of the claims.

Claims 51-65 are rejected under the doctrine of obviousness-type double patenting.

Claims 51-65 are rejected under 35 U.S.C. §103 as allegedly being obvious.

The cancellation of claims has rendered the rejections under the doctrine of obviousness-type double patenting and under 35 U.S.C. §103 moot, and it is requested that these rejections be removed.

For reasons set forth herein, all the rejections should be removed and the claims should be deemed allowable.

1. Claim 80 Satisfies The Written Description Requirement

Claims 51 through 80 are rejected under 35 U.S.C. §112, as not satisfying the written description requirement. The Examiner contends that the claims, although they require that a protein encoded by a nucleic acid that specifically hybridizes to a nucleic acid having residues 275-895 of SEQ ID NO:1 functionally inhibits proliferation of melanoma cells, do not require any particular conserved structure, and therefore "encompass a genus of molecules which potentially includes an enormous number of different species molecules."

This rejection, as applied to claims 51-79, is rendered moot by the cancellation of those claims.

Claim 80 has been amended to include a limitation that requires a conserved structure, namely a structure which binds to an antibody directed toward a fragment of SEQ ID N:2, namely the peptide Pro-Ser-Gln-Glu-Asn-Glu-Met-Phe-Ser-Ile-Arg-Asp (SEQ ID NO:5). This amendment is supported by paragraph 47, which recites a number of ways in which an increase in MDA-7 protein may be measured.

Applicant asserts that the specification fully supports and describes the use of *certain* variants of SEQ ID NO:2. With reference to paragraph 46 of the specification,

while the specification recognizes that MDA-7 protein may *essentially* be described by SEQ ID NO:2, it may vary in "insignificant ways":

> The scope of the invention embraces functional equivalents of the nucleic acid and protein which vary in insignificant ways from the native molecules; for example, it includes isolated nucleic acids which hybridize to the nucleic acid sequence set forth as SEQ ID NO:1 under stringent hybridization conditions, e.g., hybridization in 0.5 M NaHPO.sub.4, 7 percent sodium dodecyl sulfate ("SDS"), 1 mM ethylenediamine tetraacetic acid ("EDTA") at 65.degree. C., and washing in 0.1.times.SSC/0.1 percent SDS at 68.degree. C. (Ausubel et al., 1989, Current Protocols in Molecular Biology, Vol. I, Green Publishing Associates, Inc., and John Wiley & Sons, Inc. New York, at p. 2.10.3), as well as the proteins encoded by such hybridizing sequences.

What the disclosure means by the word "essentially" is evident from the last sentence of paragraph 46: "It also includes nucleic acids having essentially the sequence set forth as SEQ ID NO:1, but modified to contain restriction sites appropriate for insertion into a particular expression vector." Thus, the word "essentially" allows for minor modifications of sequence which do not affect the function of the molecule.

The Examiner has contended that altering a single amino acid can destroy the functionality of a protein. While this might be true in limited circumstances, in most cases it is not, as indicated by the numerous examples of orthologous genes shared between species, which perform the same biological functions but which, although *homologous,* differ in sequence.

In the case at hand, the express wording of the specification shows that it was not intended to be limited to proteins having *exactly* SEQ ID NO:2, nor was it intended to cover vastly different sequences. Rather, the specification requires that encompassed proteins vary in "insignificant ways" from the native sequence and are encoded by nucleic acids bearing extensive homology to SEQ ID NO:1 (as would be

necessary for hybridization under stringent conditions to occur). This is a clear and precise written description of a very limited set of variants of SEQ ID NO:2.

To hold this description inadequate would unfairly deprive Applicant of the benefit of his invention, because, if the claims are limited to proteins having *exactly* SEQ ID NO:2, to avoid infringement, a protein with as little as one amino acid variation could be used. The specification took steps to account for such "insignificant" variations, and the corresponding limitations have been introduced into the claims. Applicant has fully met the standard set forth in 35 U.S.C. §112, so that the rejection should be removed.

2. Claims 80 And 81 Are Enabled

Claims 51-81 are rejected under 35 U.S.C. §112, first paragraph, as lacking enablement. The Examiner contends that while the specification enables direct administration of the therapeutic nucleic acids, it does not enable all methods. Further, for reasons similar to those set forth in the rejection under the written description requirement set forth above, the Examiner contends that the specification does not enable the use of all nucleic acids falling within the scope of the claims.

Without prejudice to scope surrendered, the claims are amended to require that the therapeutic nucleic acids be administered by direct injection into the tumor being treated or, following tumor resection, by instillation into the tumor bed. This amendment is believed to address the Examiner's concerns, and obviate the corresponding basis for the rejection.

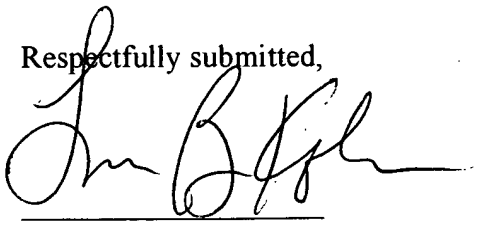
As regards enablement of the scope of nucleic acids being used, the claims are amended to require that a protein encoded by a nucleic acid which hybridizes, under stringent conditions, to the protein coding region of SEQ ID NO:1, have the structural feature of binding to antibody directed to the SEQ ID NO:2 fragment having SEQ ID NO:5, and exhibit the functional property of inhibiting proliferation of melanoma cells. For similar reasons to those set forth above, this scope is fully enabled by the specification. A skilled artisan, without undue experimentation, would be able to collect nucleic acids that hybridize to SEQ ID NO:1 and test whether protein encoded by those nucleic acids would bind to antibody directed toward SEQ ID NO:5 and inhibit melanoma cell proliferation.

Accordingly, the rejection should be removed.

3. **Conclusion**

For the foregoing reasons, it is respectfully requested that claims 80-81 be allowed. An early allowance is earnestly requested.

Respectfully submitted,



Lisa B. Kole
Reg. No. 35,225
(212) 408-2628

BAKER BOTTS L.L.P.
Attorney for Applicant